REMARKS

Claims 37-39 are currently pending.

With entry of the instant amendment, claims 37 and 38 have been amended. The amendments add no new matter and are supported in the application. Claim 37 was amended to recite ovarian cancer cells comprising cells in which 3q26.3 is amplified. Support can be found, *e.g.*, on page 32, lines 28-29. Claim 37 has also been amended to recite an inhibitor that inhibits PI3 kinase enzymatic activity. Support can be found, *e.g.*, on page 24, lines 7-8, and page 24, lines 14-15.

Claim 38 has been amended to recite that the non-peptidic inhibitor inhibits PI3 kinase phosphoinositide phosphorylation activity. Support can be found, *e.g.*, on page 10, lines 7-8.

The amendment to the specification removes a hyperlink and corrects a typographical error.

For convenience, the objections/rejections will be addressed in the order presented in the Office Action mailed April 10, 2003.

Objection to the specification

The Examiner objected to the disclosure because it contains an embedded hyperlink. This has been deleted in the amendment to the specification. Applicants therefore respectfully request withdrawal of the objection.

Inventorship correction

The Examiner notes that the request to correct inventorship contained an executed declaration by only two of the inventors. The Declaration that was submitted with the request to correct inventorships inadvertently omitted the signatures of the originally named inventors. Applicants submit herewith a corrected Declaration providing the signatures of the originally named inventors.

Rejection under 35 U.S.C. § 112, first paragraph--enablement

Claims 37-39 stand rejected as allegedly not enabled. The rejection alleges that the specification does not reasonably enable a method of inhibiting the pathological proliferation of ovarian cancer cells comprising a dose of any inhibitor of any PI kinase. To the extent that the rejection applies to the amended claims, Applicants respectfully traverse.

The claims have been amended to recite ovarian cancer cells that have an amplification of 3q26.3 and administration of a compound that inhibits PI3 kinase protein enzymatic activity. The specification indicates that a number of different PI3 kinase inhibitors, *e.g.*, polypeptides, nucleic acids, non-peptide inhibitors of enzyme activity (page 24, line 15) can be used. The current claims relate to those inhibitors that inhibit activity of the gene product, *i.e.*, that inhibit the activity of the enzyme.

Applicants disagree with the rejection for reasons of record. In brief, Applicants discovery is the involvement of PI3 kinase in the ovarian cancer cells that harbor amplified 3q26.3. Although the Examiner cites Fry (*Breast Cancer Research* 3:304-3112, 2001) as teaching that administration of the PI3 kinase inhibitor wortmannin does not correlate well with inhibition of PI3K activity, there is no evidence that the examples cited by Fry relate to the claimed cell population.

As previously noted by Applicants, a demonstration that the inhibitors work well is not required for patentability. In addition, Applicants are not required to teach the mechanism of action by which a PI3 kinase inhibitor such as LY294002 inhibits PI3 kinase. PI3 kinase inhibitors are known, regardless of whether there mechanisms of action have been delineated. Applicants have shown that targeting PI3 kinase reduces pathologic proliferation of this ovarian cancer cell population *in vivo*. Accordingly, based on Applicants discovery and in view of the teachings in the specification, one of skill in the art can target PI3 kinase as a therapeutic intervention in ovarian cancers with this amplification with a reasonable expectation of success.

With regard to the assertion that the claims are not enabled because they read on gene therapy, the current claims relate to inhibitors of enzymatic activity. The specification indicates that nucleic acid inhibitors are considered in a separate category relative to inhibitors of

enzyme activity, peptidic or non-peptidic (*see, e.g.*, the specification on page 24, lines 14 and 15; and page 23, lines 23 and 24).

Thus, in view of the reasons previously presented by Applicants and the additional arguments presented above, the claims are enabled. Applicants therefore respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph--written description

The rejection alleges that the claims lack adequate written description support. To the extent that the rejection applies to the amended claims, Applicants respectfully traverse for reasons of record. In brief, Applicants are not required to describe that which is known. Further, as noted above, Applicants are not required to described the mechanism of action of PI3 kinase inhibitors. As the Examiner notes (page 10), the synthetic peptide DQ 65-79 inhibited PI3 kinase *in vitro*. This is structurally different from LY2940002. Thus, a wide variety of PI3 kinase inhibitors with different structural features can be used in the invention. In view of the knowledge of PI3 kinase inhibitors in the art, the specification adequately describes the invention. Applicants therefore respectfully request withdrawal of the rejection.

The Examiner contends that the arguments provided by Applicants relating to potential side effects on non-cancerous cells are moot because this was not an issue in previous office actions. However, Applicants note that it was raised by the Office previously, *e.g.*, in the Office Action mailed December 14, 2002.

Rejection under 35 U.S.C. § 112, first paragraph--new matter

The claims were rejected as allegedly introducing new matter relating to 3q26. The claims have been amended to recite cells in which 3q26.3 is amplified. Applicants therefore respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, second paragraph

The claims were rejected as allegedly indefinite in the recitation of "comprising cells" and the amplification of 3q26. Applicants believe that the rejection has been obviated by the amendments to the claims.

Rejection under 35 U.S.C. § 102(b)

Claims 37 and 38 were rejected as allegedly anticipated by U.S. Patent No. 5,378,725. The Examiner contends that amplification of 3q26 is an inherent property of ovarian cancer cells, and that because the patent suggests use of a PI3 kinase inhibitor compound in neoplasms such as ovarian cancer, this disclosure anticipates the invention. Applicants respectfully traverse.

The Examiner cites Sonoda *et al.* as teaching that the most frequent sites of amplification of genes in ovarian cancer include 3q26.3. However, Sonoda *et al.* do not teach that every ovarian cancer has this amplification. Indeed, only 36% of the 25 malignant ovarian carcinomas had this amplification (*see, e.g.*, page 322, second paragraph in the RESULTS section). Furthermore, the specification does not teach that this is a property of every ovarian cancer, it merely discloses that the paraffin-embedded samples evaluated in the first example had this amplification.

In order for the amplification to be an inherent aspect of ovarian cancer, all ovarian cancers would have to have the amplification. They do not. U.S. Patent 5,378,725 does not teach the ovarian cancer cell population delineated in the claims. Thus, it does not disclose each element of the invention. Accordingly, it does not anticipate. Applicants therefore respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 102(f)

The claims were rejected as allegedly not invented by Applicants based on the deficiencies in the Declaration submitted with the request to correct inventorship. Applicants have included a proper Declaration to correct the deficiency noted in section 4 of the Office Action.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Jean M. Lockyer, Ph.D.
Reg. No. 44,879

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
JML:jml
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